AGING

KALLURI SUBBA RAO

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Popular Science

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Preface

When the National Book Trust, India first approached me for writing a book on aging meant for readers with understanding of science upto class eight, my first reaction was not a very positive one. Why should a topic like aging be discussed, I wondered! But then, I was reminded of a comment by a friend, "We begin to age the minute we are born!" Just as the phenomena of birth, growth and development are taught in schools, it is probably equally important that young students should be familiarised with the science of, the not so welcome, phenomenon of old age and senescence. After all, one of the futures of youth is old age! I have therefore undertaken the task of describing, in a simple uncomplicated language, the process of aging. Though, I must confess, that this has not been an easy task. Old age and senescence are such complicated phenomena that to put them in simple language has meant taking away all the mystic of those events which constitute life and make it sound like a straight-forward and well-understood fact of life.

I have tried my best to overcome the difficulty and make the reading an interesting one, not only for those who have studied science till class eight, but also for those who have no formal background of science, but want to know more. I do hope this book will arouse sufficient curiosity and attention among the readers to the miraculous transformation of a youthful vibrant person to a less competent 'old' one. Aging, after all, is not simply a random event of wear and tear. On the contrary, the

clues to both aging and death lie deep in our genetic blueprint.

I would like to express my gratitude to two persons, Ms N.S. Raji and Dr Sripad Gunwar, who have helped me in more than one way in preparing this manuscript. A number of the cartoon drawings were generously prepared by Mr B.V. Sathyamurthy, Hyderabad, in spite of his busy schedule, but unfortunately the publisher decided to get them redrawn. However, my sincere thanks go to him.

1

THE MARCH OF TIME

I don't want to see anybody
and I don't want anybody to see me.
You don't know what it is
to be as old as I am.
Do you suppose I want
the great GBS to be remembered
as a doddering old skeleton?

— *George Bernard Shaw*

Aging and death have always been a question mark for mankind without ever providing the exact answer as to why it should happen, why man cannot stay young forever and be immortal. Inevitability of decline in physiological functions and awareness of death have long been a major infiuence in different religions and philosophical systems.

Aging is a normal part of the life span. It is associated with a gradual reduction in the reserve capacities of most of the organ systems of the body. In other words, we can define *aging* as a process characterised by progressive decline in all physiological functions. In a philosophical sense aging starts as soon as an organism is born. However, in a different sense and in accordance with the above definition, it starts at a particular time during the life span of an organism. Aging in the human being results from the complex interplay of physiological, psychological and social factors. The understanding and control of all factors contributing to the ending of life span

has been termed *gerontology.* Every species has its life span appropriately related to its reproductive life span and the course of development. Hence, to study aging we need to know three aspects of life: *longevity, aging* and *death,* where longevity is the span of life of an organism, aging is a sequential change leading to debility, disease and death and finally we have the term *senescence* which consists of these manifestations of the aging process. Features such as aging characteristics, constitution, physical factors, diet, diseases, environmental and genetic factors, affect the aging process.

It is a common experience in our day-to-day life that when we come across another person, we are able to estimate the approximate age of that individual. How is it possible? This is because of the information accumulated in our mind about how a person looks like at a particular chronological age of his/her life. As a result of this information input into our brain, we can almost guess how a ten year or a sixty year old person looks like. The

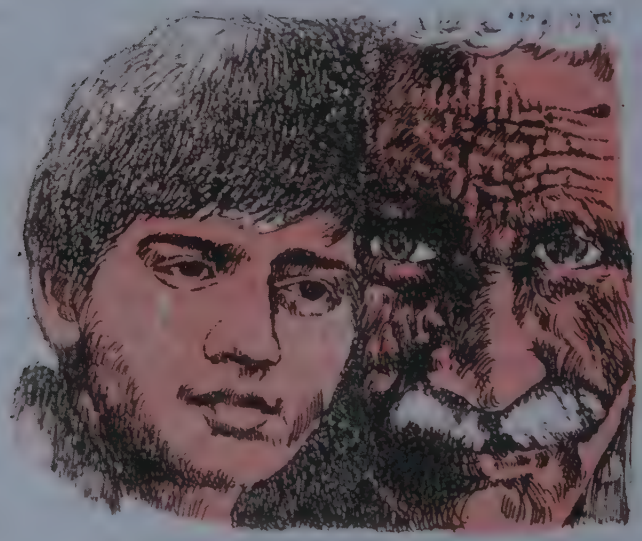

Fig. 1 showing the two faces of aging.

progressive changes that occur with age in bodily measurements and other morphological features have been recorded or experienced so well by us.

Thus it is also clear that apart from the physiological functions mentioned in the above definition, certain morphological features are also known to take place with age. To emphasise this point, two faces are shown in Fig. 1.

On the left side, a young and on the right side, an old person. The differences in the general appearance and that of the skin foldings are obvious. In our day-to-day life these appearances are taken for granted as a natural happening. But if one were to ask what mechanism is responsible for this transformation of the skin with age—the subject becomes science of aging.

Signs of aging appear at a specific time in one's life. Each sign indicates the malfunctioning of one vital organ or the other. As a final outcome, death ensues. Such is the way of nature.

Nature seems to act as an eliminator, but only after ensuring that the species has propagated itself. That is, after the function of reproduction has been completed and young replicas of the adult have appeared.

If living things do not subsequently age and die, the earth would be filled with living ones and their survival, irrespective of their age, would be threatened.

It is important to go back to the question as to when does the actual process of aging start in one's life. Before we consider this aspect it would be appropriate to review the existing knowledge about the origin of life itself and the emergence of living organisms and some facts about their life span.

Experts believe that 'life' on our planet earth began about three to four billion years ago. This 'life' began through an interaction between certain chemical substances called *nucleic acids* and *proteins*. Nucleic acids and proteins themselves must have been formed from nitrogen (N_2), ammonia (NH_3), carbon monoxide (CO), carbon

dioxide (CO_2), methane (CH_4) and water (H_2O), present in the atmosphere and deriving the needed energy from heat, electrical discharges and ultraviolet (UV) light. The products of such spontaneous discharges are thought to be *amino acids, formaldehyde* and *hydrogen cyanide.* In fact, scientists have shown the above transformations in the laboratory by itself simulating the *prebiotic* (before life began) conditions. Extensive experimentation also showed that indeed *purines* and *pyrimidines* (the nitrogen containing bases that we know today which form the structure of nucleic acids) can be synthesised starting from substances like ammonium cyanide. Similarly *ribose,* a five-carbon sugar present in one of the nucleic acids, can be synthesised from formaldehyde. The synthesis of the elementary building blocks of nucleic acids and proteins (purines, pyrimidines, sugar, and amino acids) can readily be demonstrated in aqueous solutions of simple molecules like cyanides, formaldehyde and methane known to be abundant in outer space.

The next step leading to the eventual formation of nucleic acids and proteins, namely the formation of *nucleotides* (purine or pyrimidine + sugar + phosphate) and *peptides* (amino acids linked to one another) has also been demonstrated in the laboratory. It is supposed that some minerals like zinc and lead might have once served as catalysts for polymerisation of nucleotides into nucleic acids.

Synthesis of *polynucleotides,* even before 'life' began, may have been influenced by the interaction of nucleotides with peptides. Although arguments are still on, whether protein came first or the nucleic acids, it seems that some peptides must have aided the formation of polynucleotides from nucleotides. Thus, nucleic acids and proteins, the prime molecules of 'life', seem to have formed under prebiotic conditions.

Once the nucleic acids and proteins were formed, these molecules could have aided each other to form more

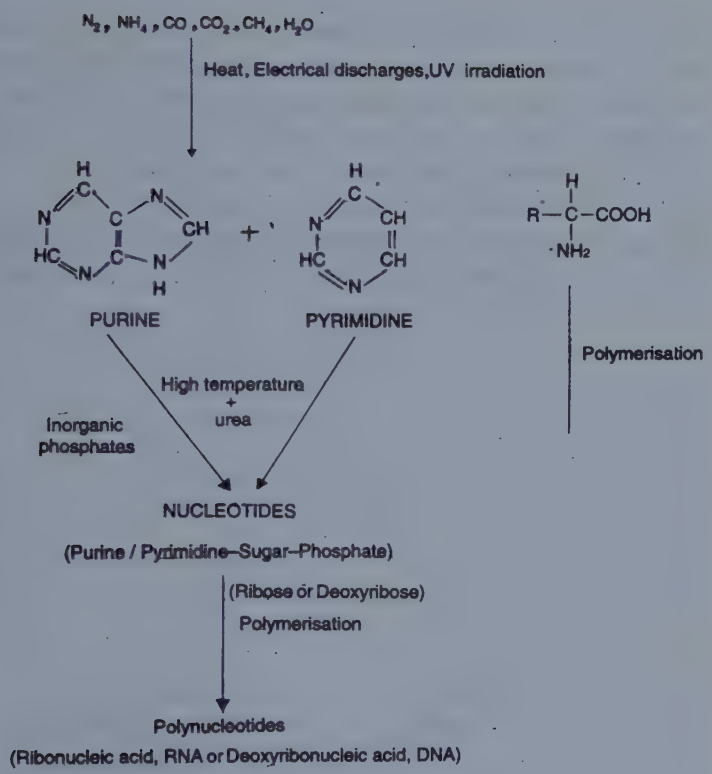

Fig. 2 showing the interactions.

of these molecules. At some point during the evolution, spanning millions of years, the nucleic acids have become organised into what is described today as *genome*, the genetic apparatus, carrying the blueprint to form copies of the original and thus propagate species.

It is still a matter of speculation as to how *inanimate* molecules like nucleic acids and proteins become 'live' and how 'life' originated. However, close examination of all 'living' matter reveals certain characteristic features of all living beings. The functional unit of the living organism is a cell with discrete chemical composition. Not only a number of diverse chemical substances are found in cells, but they exist in a highly *organised* manner. It is this

organisation of otherwise inanimate chemical substances that contributes to life. Every part and every chemical found in a living organism has a specific purpose and function. The chemical composition of a living organism is quite different from that of the environment in which it lives. The most extraordinary feature of living organisms is their ability to reproduce themselves with perfect accuracy. Not once, but countless number of times.

2

GO FORTH AND MULTIPLY

It is indeed remarkable that every living organism passes on specific characters from generation to generation. In each generation it ensures growth, development and reproduction to be followed by aging and death.

A scientist by the name of Avery and his co-workers were the first to demonstrate in 1944 that deoxyribonucleic acid (DNA) is the genetic material responsible for carrying the information from parent cell to the daughter cell.

Fig. 3 showing the DNA structure.

Another milestone in understanding the mechanism of transfer of genetic information was the elucidation of the structure of DNA by Watson and Crick in 1953, who said that DNA is made up of sugar molecules linked to a nitrogenous base and a phosphate group. The nitrogenous bases are of four types—adenine, guanine, cytosine and thymine. Each unit of the DNA molecule is a nucleotide made up of its three basic components—the base-sugar-phosphate. These units are linked together to form long nucleotide chains *(polynucleotides)*.

DNA generally exists as a double stranded helical structure (Fig. 3). The two strands are held together by weak bonds between the bases. The base adenine always forms bonds with thymine and guanine with cytosine. Thus the base sequence of one strand is always *complementary* to that on the other strand. It is the base sequences which are the actual messages for the growth and development of the organism. Each organism is unique in itself in the sense that the sequence of bases found in DNA is specific for each species. This means that each type of unicellular organism that has emerged, in the course of evolution has a characteristic type of DNA and therefore characteristic types of proteins and other molecules that are formed in the cell. It is estimated that the bacterium E. coli has about 3,000 proteins in it. A human being has about 100,000 different proteins in his body.

Considering the number of species of living organisms that exist on earth (more than a million), the enormity of different kinds of proteins and other molecules that exist in the living world could be imagined. The point to note here is that this enormous diversity owes its origin to the diversity of the base sequence in DNA, and to the mystical manner in which this chemical changes its sequence of bases during the process of evolution.

One of the outstanding properties of a living being is to reproduce in a faithful manner. This means that the daughter cell would have an exact copy of the genetic material, the DNA, which in turn means that the sequence of the bases in DNA of a daughter cell would be the same as in the parent cell.

Let us see how the primitive unicellular organisms achieved their replication. The most ancient, smallest and simplest living organisms are the microscopic, unicellular beings called bacteria. Bacteria are found everywhere where life can be supported. Bacteria normally reproduce by the *asexual* method described as binary fission.

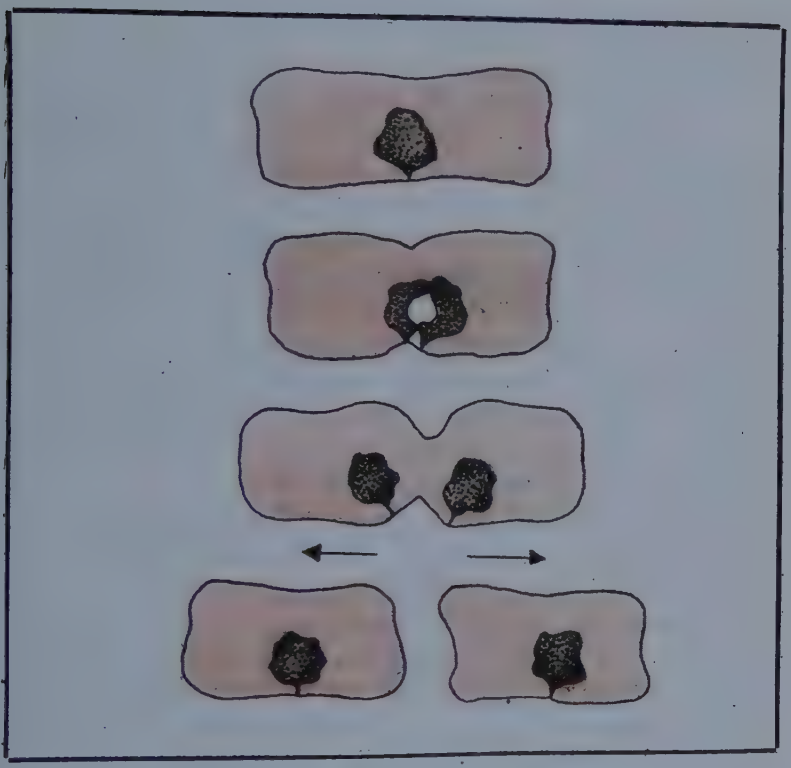

Fig. 4 showing binary fission.

During this process, the genetic material (DNA) first duplicates itself. Subsequently, the cell itself expands and divides into two with the formation of a new cell wall in the middle. Thus the whole cell is ultimately divided into two daughter cells with each of them having identical copies of the genetic material. In a bacterium, this division takes just about twenty to thirty minutes under ideal conditions.

A careful look at the description of asexual reproduction through binary fission should reveal the interesting point that while propagating its own species, the whole cell is dividing and no portion of the cell or the genetic material is lost during the event. In other words, there is no question of aging and death for this species

and as long as nutrients are available this mode of reproduction continues.

There are some bacteria like E. coli which exhibit a form of sexual reproduction described as 'bacterial conjugation'. During this process a donor bacterium (can be viewed as male) transfers a small piece of DNA called *plasmid* to the recipient bacterium (can be considered as female). Sometimes the plasmid contains a specific gene called the fertility or F gene. Such a bacterium assumes the role of a donor or male. During the transfer of plasmid from donor to recipient, it is sometimes possible, that a portion of the donor's chromosome is also transferred to the recipient. This process of transfer of plasmid at times along with a small part of the chromosome is known as *conjugation.* Following this, the recipient bacterium undergoes division and gives rise to progenies which would inherit some of the properties of the donor.

Thus once sexual reproduction sets in, no matter how primitive the organism might be, its progenies always acquire a mixed genetic character and the daughter cells are no longer a true copy of the parent. Moreover, after donating its genetic material to the recipient bacterium, the donor bacterium has no further role to play!

Another deviation from normal asexual reproduction is the formation of spores in bacteria. This is to protect the genetic material of the cell from adverse conditions of environment. During spore formation bacteria form an impermeable coat around the genetic material and some protoplasm (Fig. 5). The rest of the cell degenerates. The spore remains dormant through unfavourable conditions. When a favourable condition ensues, the spores become active again and divide.

Spore formation and conjugation are examples to indicate that even in primitive unicellular organisms, there is a natural tendency to evolve towards sexual reproduction which is characterised by some special status to the genetic material so essential for the propagation of species.

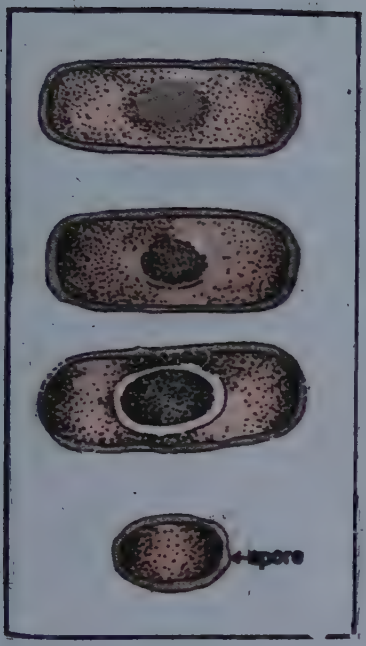

Fig. 5 showing spore formation.

In the process, nature does not seem to mind sacrificing a part or whole of the parental cell.

In multicellular higher organisms, propagation of species is always by sexual reproduction. The transmission of genetic information is a complex phenomenon and the offsprings are never a true copy of either of the parents. Further, in all such higher organisms, the parent cells or the parents themselves, die sometime after performing the reproductive function. What does this mean? As the 'life' evolved from unicellular to multicellular organisms the mode of reproduction seems to have changed from asexual to sexual. This change in the mode of propagation of species also appears to bring a new phenomenon in living beings—senescence and death.

In humans the genetic material is present as twenty-three pairs of long, coiled forms of DNA called chromosomes (Fig. 6). Twenty-two pairs of chromosomes are identical and are described as homologous. The twenty-third pair determines the sex of the individual. In males, this pair is non-homologous. It contains one X chromosome and one Y chromosome. On the other hand, in females, this pair is homologous. It contains two X chromosomes. Cells containing only one set of chromosomes are referred to as haploid while cells containing twenty-three pairs, that is forty-six chromosomes, are referred to as diploid. All the cells in human beings, except the sex cells—sperm and egg—are diploid. The

haploid sex cells or gametes are formed by a type of cell division called *meiosis*. Meiosis achieves two aims. One, it halves the chromosomal number of the diploid cells to form the haploid gamete. This is nature's idea to maintain the chromosome number of the species. When the sex cells fuse, the zygote thus formed will have exactly the same number of chromosomes as the parent. Second, is an important event called *crossing over*. During meiosis, there is an interchange of portions of chromosomes.

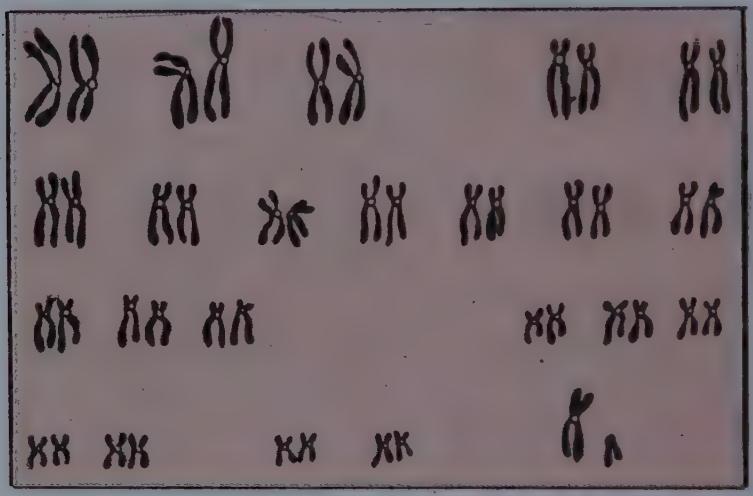

Fig. 6 showing the twenty-three pairs of chromosomes.

In sexual reproduction, during the process of formation of gametes and their fusion to form a zygote and in subsequent cell divisions to mark growth and development of zygote into an adult, countless chances occur for recombination, reassortment of genetic traits in the offspring. The crossing over of a portion of the chromosome to that of the other is both a chance and a necessity driven by yet unknown forces in order to adapt to the changing environment.

What does this mean in molecular terms? Certain base sequences in the DNA can cross over to a certain part of another chromosome—thus resulting in a variety

of assortments of genetic units in the offspring. It is this process that leads to an enormous variety of characteristic features that are noticed in individuals. When this type of crossing over occurs in a somatic cell during the mitotic division, it is referred to as *somatic mutation.* The occurrence of such mutation is generally rare in primitive organisms when the chromosomal number is small and mode of reproduction is asexual and the replication of DNA is characterised by high accuracy. However, in higher organisms like human beings, the chances are reasonably high due to the complex nature of reproduction, growth and development.

Thus, with the advent of complex sexual reproduction and complexity of genetic apparatus, the organisms have acquired during evolution the phenomenon of getting old and finally becoming vulnerable to damage and meeting death.

It is clear that nature has 'opted' for elimination of the individual organism once the duty of reproduction is fulfilled. Quite obviously, the only natural purpose of any living being is to survive and this survival is aimed only at the propagation of species.

Granting that the only purpose of a species is to propagate, why opt for the elimination of members during post-replication period? What are the advantages conferred upon species because of death?

The answers to these questions are not too difficult to guess. If living things do not disappear from the scene and continue to propagate, then the earth would be filled with such animate species and their very survival, irrespective of their age, would be threatened. There will be dreadful competition for food, shelter and other resources that are required for living.

Nature has made a choice for sexual reproduction to introduce tremendous variety in the genetic make-up. In the process, the phenomenon of senescence and death need not occur through the genetic debility that sets in

after reproductive performance, but is also caused by predators (that is one species using the other species as food). Even in this aspect, older animals are more easily killed by their predators because of the decreasing physiological and physical activities in such old animals.

Fig. 7.

3

THE ONSET OF AGE

Eighty years old!
No eyes left,
No ears, no teeth,
No legs, no mind,
And when all is said and done,
How astonishingly well
One does without them.

— Paul Claudel at 90 years of age

It is a biological dictum that the instinctive destiny of every living organism is the propagation of the species. As long as this propagation is done in an asexual manner, the aging phenomenon is not apparent. But once the sexual mode of reproduction comes into play, aging is one feature, among others, that becomes apparent. In other words, once the offsprings are produced, the system itself recognises the lack of further utility of parents and some kind of switch comes 'on' to begin the process of aging that eventually culminates in the removal of the old from the population.

Apart from the visible changes of greying hair and wrinkling skin there are other changes that occur within the body at the tissue and cellular level. In fact, the outside changes are the result of internal alterations at the cellular level. There is an overall physiological deterioration in all vital functions like respiration, cardiac function, kidney function, muscular function, etc. Although one may not realise and feel that these changes are taking place inside

Fig. 8 showing wrinkles and greying hair.

the body, if, one is subjected to a systematic test, the decline in these functions can even be observed.

Physical Changes

When a child is born and goes through childhood before he or she becomes an adult, we never describe them as 'old' although in a philosophical sense the process of 'aging' starts as soon as the ovum is fused with the sperm and a zygote is formed. The zygote divides a number of times to form a large number of cells. Then at some point these cells differentiate into different organs and finally the body is formed as we see when a child is born. These changes are declared as growth, development and maturation and there is a positive meaning attached to the whole gamut of changes.

On the other hand, when the fully grown adult gets married and begets children, at some point during this

time the symptoms of so-called 'aging' start appearing.

Grey hair make their appearance first at temples and then at other places. Some people go bald due to loss of hair in the scalp. There will be changes in the skin-fold thickness. Wrinkles appear due to loss of fat underneath the skin. The skin also becomes thin and rough. It becomes less elastic and brittle.

Some scientists compare the changes in the patterns

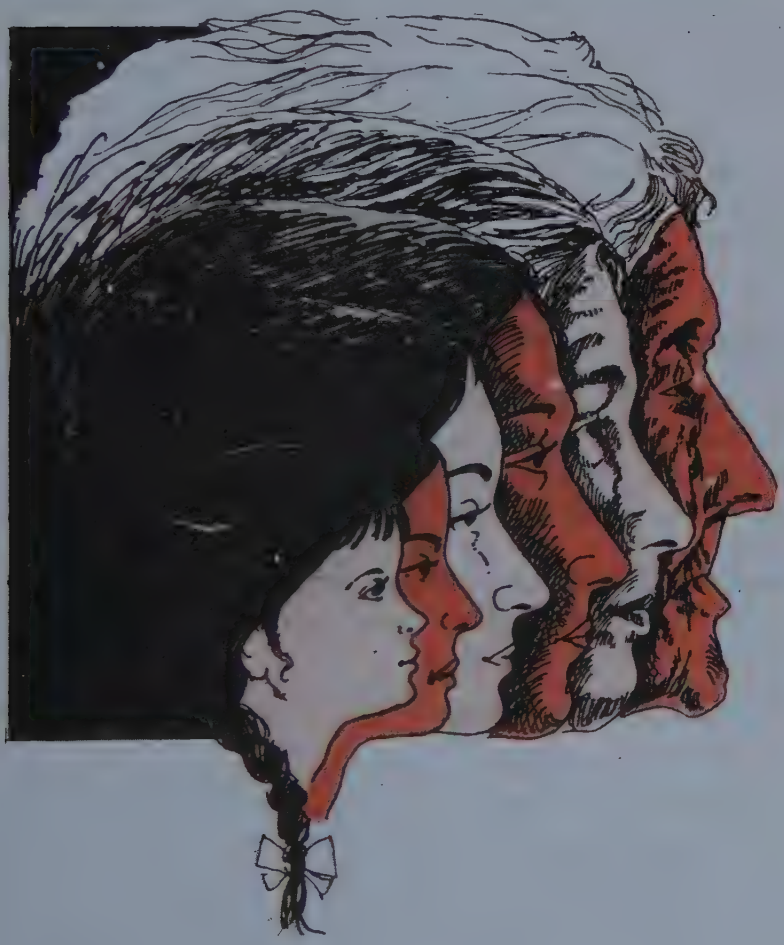

Fig. 9 showing faces at different ages.

of activity of an organism, beginning from the early stages of life until death to that of the path of a javelin when it is thrown upwards. It travels fast initially, slows down gradually, reaches a plateau and then descends, the speed of the descent increases as it nears the ground due to gravity. After birth, the growth and development of a child occurs at remarkable speed. During teenage the rate of growth starts slowing down and at about the age of twenty years it begins to plateau. The plateau extends upto the age of thirty to thirty-five years after which several symptoms of 'aging' start making their appearance slowly. The rate of this decline increases with age.

Some other scientists compare the human being to a space vehicle launched by the aeronautical engineers to fly past other planets and relay information back to earth. Scientists and engineers worry about the soundness of all the working systems until the vehicle reaches the target planet. Once the mission is completed, they worry no more about the vehicle although it continues to fly. How long will it fly? Which parts would fail first? The experimenters don't care. That is the way nature too seems to feel about us for its sole aim seems to be to propagate the species, after which aging commences.

Thus aging and the terminal point of that process, that is death, are not sudden in a normal healthy individual. The process begins around the age of thirty in humans and acquires speed with increasing age.

Changes in Body Composition, Tissues and Cells

The lean body mass consisting of muscles and tissues decreases steadily after physical maturity until in extreme old age, it may get reduced to two-thirds of adult value. Body weight, however, increases with age because stored fat and body water increase after decreasing steadily throughout foetal and post-natal development. All tissues, and even skin, become laden with water as a consequence

of aging. The loss of voluntary muscle tissues is evidently due to disuse of muscles and setting in of atrophy rather than loss of muscle fibres.

Changes that take place within the body at the organ, cell and molecular level have other consequences. The thymus gland which is responsible for protecting the body against invading foreign organisms weighs about 200-250 grammes at birth. After maturity this organ begins to shrink and by the sixtieth year is reduced to a small size of about 3 to 5 grammes. This is one of the reasons why older people fall sick more often. Once the defence mechanisms are weak, the person becomes susceptible to all kinds of infections.

The body's structure depends on two kinds of fibrous protein molecules—*collagen* and *elastin*. Collagen constitutes almost one-third of the body protein and is found in skin, bone and tendons. The rate of collagen synthesis is high in youth and declines through rest of the life. Insoluble collagen increases with age leading to rigidity and general body stiffness.

Then there are stem cells in the blood-forming tissue which respond readily to injury in youth but diminish in capacity with age. There is increase in incidence of anaemia in old age due to depletion of blood-forming stem cells.

It may be surprising that the height of an individual begins to decrease from the age of thirty. By the time one is sixty, as much as three-fourths of an inch in height is lost. The muscles also begin to lose their weight because of the degeneration of the muscle cells and which are not replaced. Slowly the space of these cells is taken by fat. According to one estimate more than half the muscle mass is lost by the time one is seventy.

The most outstanding psychological features of aging are the impairment of short-term memory and the lengthening of response time. Both these factors contribute to lower scores of elderly persons on standard tests of

'intelligence'. Age decrements are negligible on tests that depend on vocabulary, general information and well-practiced activities, but get more pronounced on tests in which associations formed early in life must be displaced by new ones.

Both hearing and vision become less efficient. It is commonly seen that people beyond the age of fifty and sixty keep asking the other person to repeat what is said. Similarly visual capacity decreases after the age of forty. The number of optic nerve fibres, serving vision, decreases at nearly comparable rate as the olfactory which decrease to about 25 per cent of the number at birth. Most people notice loss of sharpness in their close-up vision. As a result, they tend to increase the distance of the reading material. Since reading becomes difficult, reading glasses adorn the face. Reading glasses (spectacles) are nothing but a magnifying device to make reading from a particular distance easy. The lens of the eye also begins to harden. This is what is described as *cataract* marked by cloudy vision. More than 50 per cent of the population suffer from cataract by the time they attain the age of sixty.

There is a decrease in the ability to focus for long on very distant objects due to myopia. This is in part due to the weakening of the ciliary muscles of the eye, decrease in fluidity of the lens and partly because the lens which grows throughout life at a particular rate diminishes in its rate of growth with age.

Also the ability of the eye to adapt to darkness (i.e. increase its sensitivity at low light levels) decreases with age, part of which can be restored by breathing pure oxygen.

In man, the number of olfactory nerve fibres which serve the sense of smell, decrease by the age of ninety to about 25 per cent of the number present at birth. The senses of smell and taste too decline particularly during the sixth and seventh decades. Since the person is unable to appreciate the flavour of several food substances, there

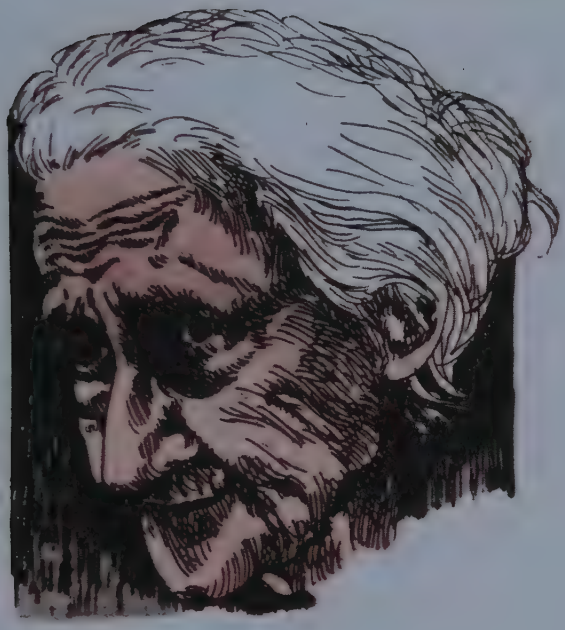

Fig. 10 showing an old woman.

is a tendency to change the dietary habits which may lead to low calorie intake—resulting in insufficient nutrition.

Sleeping habits also change in older people. The need for long sleep diminishes. They tend to sleep for shorter durations and the quality of sleep is light rather than a deep one. It is believed that these changes are due to both physiological and psychological reasons. The change in the sleeping pattern also causes psychological problems in some people. They tend to feel that they are suffering from *insomnia* (a condition of not being able to sleep) and sometimes resort to drugs.

The human body derives energy from the food that is consumed. There are a variety of chemical reactions taking place in the cells of the body to convert the food that is consumed into energy. Moreover, several other substances are synthesised in the body utilising the raw materials supplied through one's diet. All these reactions

are carried out with utmost efficiency and specificity with the help of biocatalysts called *enzymes.* These chemical conversions comprising synthesis of some compounds and degradation of others are collectively referred to as *metabolism.* The rate at which these various reactions occur is known as the rate of metabolism. The metabolic rate has a bearing on the overall growth and efficiency of the body system.

The body's metabolism begins to slow down by the age of twenty-five. After this age the number of calories (the energy content of the diet is usually referred to in terms of calories) needed to maintain the body weight decreases. According to one estimate a 2 per cent reduction in the caloric requirement occurs every ten years. However, a number of people put on fat during and after adulthood because they continue to consume excessive calories than actually needed.

The master organ, the brain, loses 20 per cent of its weight from adulthood to old age. The brain has about 10^{11} cells called neurons. After thirty or thirty-five years, these cells begin to degenerate at a rate of 100,000 per day! Since these cells are in such an excessive number their loss is not felt by a normal healthy individual. The cells still remaining take over the functions late into old age. However, closer examination reveals loss of mental functioning particularly that of short-term memory. In any case, mental disability appears to be one of the last symptoms of aging.

Effect of Aging on Body Systems

Aging brings with it a series of ailments. Quite naturally the organ's poor functioning leads to several complications.

Immunological System

An important molecular information system of the body

is the immunological system, part of which, the thymus-dependent subsystem, is specialised for defence against invading micro-organisms. The immunological system has been implicated in the body's defences against the much dreaded disease called cancer that normally afflicts older generations. Studies reveal that aged persons have greater chances of suffering from this disease. Cancer is a condition of uncontrolled multiplication of a population of cells in the body. Cancerous cells not only multiply but also invade the neighbouring tissues and thrive at their expense. Further, they travel to other parts of the body and start multiplying at a new site, which could be a vital organ, thus disrupting its activity. Extensive research is going on all over the world to find out why normal cells turn cancerous. It is believed that both cancer and aging are caused by alterations in the DNA molecule, the genetic material. It is not, however, clear which of the alterations lead to cancer and which of them to the death of the cell.

Cardiovascular System

Diseases of the heart account for over 50 per cent of deaths after the age of sixty-five. Even in the absence of detectable diseases, the heart undergoes deleterious changes with advancing age. Structural changes include a gradual loss of muscle fibres accompanied with infiltration of fat and connective tissue. The heart also shows a gradual reduction in performance with increase in age. The amount of the blood pumped by the heart diminishes by about 50 per cent between twenty and ninety years of age. Under resting conditions, the heart rate does not change significantly with age. During each beat, however, the muscle fibres of the heart do not contract as rapidly in the old as in the young. This reduction in rate of work is due to the age-associated reduction in the activities of certain cellular enzymes that produce the energy required for muscular contraction.

Arteriosclerosis, or hardening of the arteries, increases markedly in incidence with age. It is characterised by the deposition of fatty and other substances on the inner surface of the walls of the arteries. Blood vessels become elastic and there is progressive thickening of the walls of larger blood vessels with an increase in connective tissues, which become stiffer. This loss of elasticity increases with resistance to the flow of blood so that blood pressure also increases. This in turn increases the work the heart must perform to maintain the flow of blood. On the average, obese people have higher blood pressures than those with normal body weight. Since the incidence of obesity increases with age atleast upto fifty to sixty years, this factor is believed to contribute in part to the increase in blood pressure with age.

Digestive System

Loss of teeth and incidence of oral disease increase with age but with better fluoridation of water and better care of teeth during childhood the incidence of loss of teeth will decrease.

While secretion of hydrochloric acid by the stomach as also of other digestive enzymes decreases with age, the digestive system is not impaired significantly in the elderly. Some impairment in absorption of fats may occur but it is of no significant value. Deficiencies of nutrition may occur due to poor eating habits or reduced intake of protein, calcium, iron and vitamins. Nutritional deficiencies can be avoided by including adequate quantities of protein, calcium, iron, vitamin A and thiamine in the elderly person's diet, and by ensuring regular eating habits.

Nervous System

With advancing age there is a slight loss of neurons (nerve cells) in the brain which may lead to poor responses and

Plate I :
a case of Parkinson's disease.

Plate II :
a fifteen year old boy
with Cockayne's syndrome.

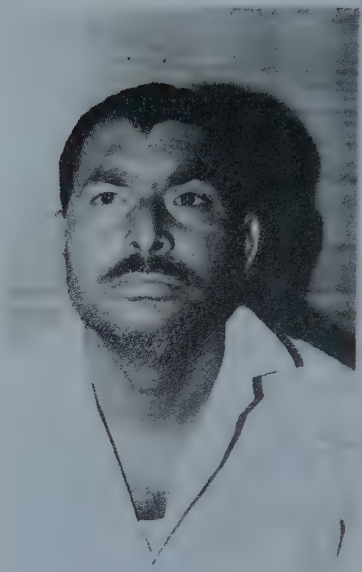

Plate III :
a victim of dementia.

Plate IV :
a forty-eight year old woman
with Werner's syndrome.

Plate V :
a girl with progeria at the
age of five years.

memory defects. Since enough is not known about the brain, one cannot say with certainty that there is some connection. Even centenarians are known to have an adequately functioning nervous system. There is a general slowing of responses in the elderly; reflexes become more sluggish and the speed of conduction of impulses in the nerves gets slightly slowed down.

Similarly, there are a number of nervous disorders more commonly making their appearance in persons beyond fifty or sixty years of age. These include Parkinson's disease (Plate I), Alzheimer's disease, senile dementia (Plate III) and stroke.

Parkinson's disease is featured by uncontrolled contractions of skeletal muscle, causing tremors. The person experiences difficulty in initiating movement and then moves slowly while leaning slightly forward. Speech is slow. The disease is a chronic and progressive one and for some yet unknown reasons more common in men than women. This disease is caused by the degeneration of an area called *basal ganglia* in the brain. The most effective treatment for this condition is the administration of a compound called L-dopa.

Among the earliest symptoms of Alzheimer's disease are impairment of recent memory, spatial disorientation and a lessening of spontaneous emotional responses. Gradually hearing functions deteriorate and the ability to read, write and calculate are lost. The patients become very confused and cannot even recognise members of their family. The patient may in the final stages experience seizures and cannot speak even. All these symptoms are collectively referred to as *dementia* (mental deterioration). Considerable research is going on to understand the genetics of this disorder and to prevent it. While this disorder seems to be quite prevalent in white populations, no reliable data on the incidence of this disorder in India are available.

Senile dementia, as the name itself indicates, is the

deterioration of mental functions in old age. The symptoms of senile dementia are quite similar to those of Alzheimer's disease except that senile dementia does not become apparent until after the age of sixty-five.

Cardiovascular accident or stroke is a common aging dysfunction. A stroke occurs when a blood vessel to the brain gets obstructed or ruptured. Blood supply to that region of the brain gets affected causing brain damage. The neurological effects of stroke vary from one case to the other depending upon the site and extent of damage. Paralysis, seen quite often in old people, is the result of stroke. In severe cases, death may result.

Endocrine System

Hormones are very important in the regulation of many physiological systems. Impairments in endocrine glands were believed to be a cause for aging, but it no longer holds true.

However, it has been identified that the hormone insulin, secreted by the pancreas, helps in regulation and utilisation of sugar and other nutrients in the body. When the pancreas fails to produce adequate amounts of insulin, *diabetes* occurs. In other words, the cells are unable to utilise the glucose for energy and other purposes. This may be due to either insufficient production of insulin, that helps to convert glucose into energy in cells, or due to malfunctioning of the hormone as a result of which it is unable to make the cells take up glucose and metabolise it. Either way high levels of glucose and sometimes even that of insulin are found in blood. Since glucose is not available, the cells end up using fat and proteins for energy and this leads to a variety of complications. Although one form of diabetes is found occasionally in young people (the juvenile type of diabetes), more often this disease is associated with advancing age.

Reproductive System

The secretion of both the female sex hormones (estrogens) and male sex hormones (androgens) reduces gradually over the age span fifty to ninety years. Though diminishing sexual activity does occur in both males and females there is no uniform or hard and fast rule; it varies with individuals.

Skeletal System

Due to aging, the bones lose calcium and minerals and are more prone to break even with minor falls. Healing of fractures is also slower than in the young. Osteoporosis or loss of calcium and minerals, is more common in females after menopause and is especially evident in the spinal column. All kinds of back pain are a primary symptom of the disease which can be treated with increased intake of calcium and anabolic hormones. The ability of joints decreases with age and the incidence of arthritis increases.

Respiratory System

With age, the capacity to expel air from the lungs after a maximum inhalation decreases due to the stiffness of the bony cage of the chest and the decreased strength of the muscles that move the chest during respiration.

Emphysema (abnormal distension of the lungs with air) is a lung disease with high incidence between the ages of forty-five and sixty-five; the same holds true for *bronchitis* (inflammation of the bronchi) too.

Kidney

The kidney removes waste from the body by separating them from the blood and forming urine. With advance in age, the concentrating ability of the kidneys falls, such that more water intake is necessary to flush out the waste.

Fig. 11.a. showing the alarm clock in the aging process.

The reduced concentrating ability of the kidney results from a loss of some of the nephrons, the functional elements of the kidney, and the reduced activity of cellular enzymes.

It is quite obvious that the process of aging is not sudden but actually starts during the reproductive period, and continues at an increasing rate with time. At some stage of this debilitative process, the body can no longer manage to sustain the vital activities, thus leading to senescence and finally death.

Can we then compare the aging process to a clock? Indeed there appears to be an in-built biological timer which tells the various organs and cells, after thirty or

forty years of age, that their time is up. Much like the setting of an alarm clock to ring at a specific time, the body too has its time when deterioration begins.

On the other hand, one can also see the in-built timer as a tightly wound spring of a clock. Aging would then be like a slow unwinding of the spring and after a time, the spring becomes quite loose and the clock begins to show erratic time and finally stops.

Scientists have been tinkering with the human body, down to its molecular level to unravel the mysteries of this ticking.

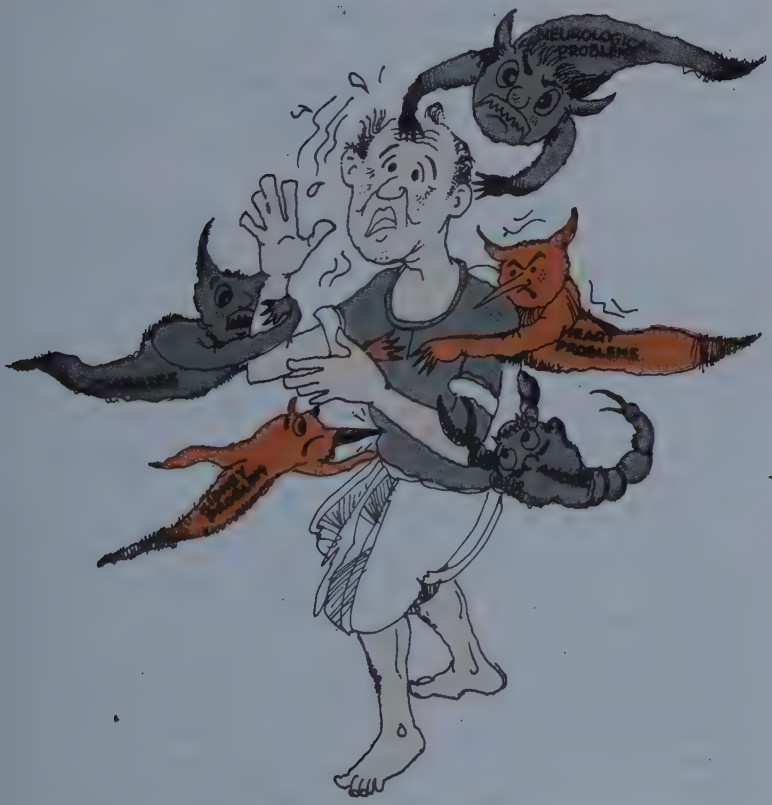

Fig. 11. b. showing an old man with various diseases attacking him.

4

THE KEY TO THE CLOCK

Pray, do not mock me.
I am very foolish, fond old man,
fourscore and upward,
not an hour more or less.
And, to deal plainly,
I am not in my perfect mind.

— *Shakespeare in* King Lear

"His wife looks so much older to him!" "He has grown old so rapidly in the last few months!" We often hear these comments from people which are indications that the alarm clock has been triggered. Just what triggers the alarm clock or the unwinding of the spring? In a quest to find an answer to precisely this question, scientists have been analysing the changes that take place within the body. A number of scientists have proposed theories or the possible reasons for aging.

Most theories of aging are based on changes in three basic biological components of our body. One is those cells of the body that divide and produce new cells as long as the person is alive. This is true of most of the various types of body cells; another type of cells are that actively divide during early embryonic stages, but stop dividing after birth. Such cells are commonly referred to as post-mitotic cells, since they have undergone the last mitotic division of their lives and are no longer capable of undergoing mitotic division. Nerve cells and skeletal muscle cells are typical examples of this type. The body

also has large non-cellular areas in between the cells composed of the intercellular substances which form the third component. The protein, collagen, is one main intercellular substance. It provides support in the skin, cartilage, tendons and other such connective tissues.

These three components are subject to physiological controls that are operative in the body. Some feel that the changes in the dividing cells are important while others believe that changes in non-dividing cells are more important.

Broadly the various theories of aging put forward till today can be classified into two categories—those who believe that we are preprogrammed to age at a specific time in our lifetime and those who suppose that aging is stochastic or spontaneous in nature as a result of random events that take place in the body with time. Quite often theories in one category overlap with those in another.

In general all theories that fall under 'programmed aging' are influenced by the fact that different species of organisms have different life spans and all individuals within a species have a more or less similar life span. For example, mayflies live only one day, houseflies thirty days, rats three years, dogs twelve years, horses twenty-five years, elephants sixty years and men seventy years. If you give each week in a rat's life the value of six months in a man's, the aging process runs parallel in the two species. Similar comparative scales can be made between any other two species. This means that the three main phases of life are there in every species—development, reproduction and senescence. The only difference is in the length of each phase. For instance a rat after birth thrives on its mother's milk for about three weeks. From then onwards it can eat outside food independently to become an adult by three to six months of age. The reproductive period spans for about six months at which point aging symptoms begin to appear.

Usually this animal dies any time after two years.

A human baby thrives on mother's milk for about six months and quite often this continues upto one-and-a-half to two years. Adulthood is reached by twenty years. Reproductive phase spans for another twenty years, then signs of aging appear. The point to be noted here is that the *milestones* of life are the same in all species. However, the time taken to cross each milestone varies and apparently this is what determines the life span.

Humans and other animals which live long take more time to reach reproductive maturity. What determines the length of the developmental period and of the reproductive period? Obviously during evolution these characteristics are gained and therefore, the determinants are genetic in nature, meaning, the life span is programmed in the *genes*.

The belief that both, the phenomena of aging as well as the fixed life span for different species, have a genetic basis—has received a tremendous stimulus following a very important discovery by an American scientist, Leonard Hayflick about thirty years ago. It was once believed that cells grown in laboratory cultures are essentially immortal once the nutrient supply is ensured. But Hayflick showed that this applies to only malignant or cancerous cells.

Normal diploid cells when cultured in a petri dish in the laboratory under appropriate conditions, grow until they cover the whole surface of the container in a monolayer. When they reach this stage, they are said to have reached *confluence*. If a portion of these cells are now taken out and placed in a fresh container having appropriate medium to support growth, once again they grow until they reach the confluence. This process constitutes a *passage*. If half of the confluent cells are transferred to a fresh container in this way, it is referred to as a 2:1 split. That is, the cell will be expected to double at each passage.

What Hayflick and his co-workers found was that

when they cultured the *fibroblasts*, a type of cells from human foetal tissue, in the above manner, the cells went through fifty doublings and then stopped, irrespective of how adequate the fresh medium to which they were transferred to. The cells showed signs of senescence and death. This meant that human foetal fibroblasts can undergo division fifty times and no more. While some cells during these passages showed signs of aging and died due to a variety of other reasons, the cells which continued to divide and grow did so until fifty divisions. Excitement grew when it was observed that if an embryonic cell divided say twenty times and then put into a freezer for months or years, the cells actually remember where they left off! If brought back to room temperature and cultured, they divided another thirty times and no more!

Not only that, when the cells were taken from older individuals, they divided fewer times and then stopped. This meant that the number of doublings a cell can go through is dependent upon the age of the donor. Older the donor, lesser are the doublings. These experiments have clearly shown that the information regarding the number of divisions a given cell can go through is already written in that cell. This is *Hayflick's limit* or the *maximum life span*. Many theories have emerged to explain this genetically programmed maximum life span of different species.

On the other hand, the stochastic theories of aging predict that the aging process can be influenced by random events that take place inside the body as well as outside, for example, exposure to radiation, dietary habits and climatic conditions. However, it is also possible that these factors only modulate the process and the inherent capacity of the organism to cope up with these events still remains at the genetic level. Thus, as already mentioned at some point, some of these theories converge to a genetic basis.

For any aging theory to be valid, it must satisfy three criteria—the changes that the theory attaches importance to must occur in all the individuals of a given species; the change(s) must be progressive with time; and the changes must lead to dysfunction of an organ or a system in the body.

Let us take a look at some of these theories.

The Death Gene Theory : This theory proposes that aging is genetically programmed through one or more of the harmful genes in an organism. These genes become active at a particular time in late life and alter the physiology of the organism in such a way that death results. Recall the analogy of an alarm clock that begins to buzz at a predetermined time. Here the alarm clock is like a *gene(s)* which becomes active at a predetermined time in the life span. It is also possible that these genes are active even during the early years but are altered in later years, thus switching their function. In the altered state the genes may be responsible for the functional decline and structural changes associated with aging. This theory suggests that the human life span is an inherited trait. There is some support to this concept.

Studies with twins have shown that there is considerable similarity in age of death of *monozygotic* (where a single egg splits to form two individuals) twins, whereas this similarity is not that apparent in the case of *dizygotic* (where two eggs develop together) twins. Survey studies also show that in general the offsprings of long-lived parents have a longer life span. This concept is also supported by reports claiming extraordinary longevity of people residing in certain mountain regions like Vilcabamba in Ecuador, Humza in Pakistan and the Abkhasia region of Soviet Georgia. In these regions, people are known to live upto 120 years!

Finally, the recent identification of some genes in cultured cells that are capable of inducing senescence

when introduced into normal healthy cells is a shot in the arm for believers of this theory since it does prove the existence of information at genetic level to induce aging and senescence. However, it must also be admitted that the manner in which the genetic signals are actually transformed into visible aging is far from understood.

Gene Regulation Theory : This theory was proposed by an Indian scientist, Prof. M.S. Kanungo of Benares Hindu University almost twenty years ago. He has attempted to explain two important features of aging—one is the gradual decline in adaptation to environmental changes after attaining reproductive maturity and second, the approximate fixed life span of the species. According to this model, senescence may result from changes in the expression of genes after reproductive maturity is reached. There is a sequential activation and repression of genes through the three phases of life—development, reproduction and senescence. In simple terms, some of the genes which are active during development may activate some genes which would induce the reproductive phase of life. Once again some of the genes which are active in reproductive phase would induce some other genes which are responsible for the onset of senescence.

In this model the reproductive phase occupies a significant part of the life span which, in the case of many mammals, is true. This theory also emphasises, like many others, that the length of developmental and reproductive phases, as evolved, has a relation to the life span of that species. The validity of this theory lies in the identification of the precise gene products of one phase which triggers the next phase. Scientists are at it.

Codon Restriction Theory : The theory proposed by American scientist, B. L. Strehler states that aging occurs due to a malfunction in the most essential act of the cell—that of protein synthesis.

All information regarding structure and function of an organism is stored in the genetic blueprint—the DNA. These functions are mediated through proteins.

Proteins are long chains of various combinations of the twenty different amino acids. The exact sequence of the amino acids for each protein is coded on the DNA. During synthesis, the information on the DNA is copied on to a messenger molecule which is a ribonucleic acid (RNA) called messenger RNA (mRNA). This is done through a process called transcription where, for every three bases of the DNA that carry a message, an mRNA with complementary bases is formed. These are called the *triplet codons.*

The mRNA is then translated into protein. This

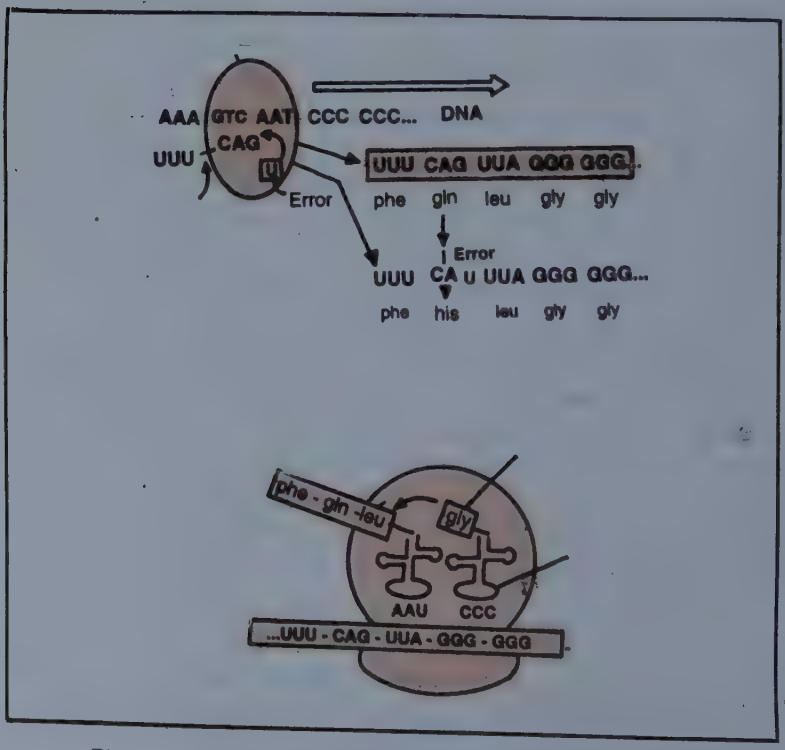

Fig. 12 showing DNA-RNA protein information transfer.

information transfer is based on the language of triplet codons. For example, if the mRNA has triplet codons like Uracil-Uracil-Uracil (in short written as UUU) then it codes for the amino acid phenylalanine. Such codons are there for all the twenty amino acids usually found in body proteins.

So the original information or direction residing in DNA is passed on to proteins via the mRNA molecules. Proteins are like soldiers who do their duty in a highly disciplined manner after getting the instructions from the supreme commander, the DNA, through the intermediary officer, the mRNA.

The codon restriction theory is based on the assumption that the accuracy with which the triplet codons in mRNAs are translated into amino acids is lost with age. There is some experimental evidence to show that it is indeed so. However, why this happens is not clear by any of these experiments. It is also possible that this defect could be an effect rather than cause of aging. Therefore the basic question remains unanswered.

Somatic Mutation Theory : This is another theory which seeks to explain the basic reasons for the changes that occur with age. The starting point that led to the proposal of this hypothesis was an experiment by a scientist, L. Szilard in 1959 who reported that rats exposed to radiation (X-rays, γ-rays, ultraviolet light) died at a younger age than non-exposed animals. These observations were extended to humans by other scientists later. A higher cancer incidence was noticed in irradiated individuals suggesting that radiation exposure accelerates the aging process. From these observations the theory emerged that exposure to radiation damages the structure of DNA, the genetic blueprint. Because of this damage or alterations in DNA structure, there occurs a progressive loss of essential genes which would ultimately result in decreased production of functional proteins and at a critical level, cell death.

While there is some evidence to show that X-ray irradiation shortens life expectancy in some species, the difficulty arose when these observations could not be confirmed uniformly in other species of animals. Also, several chemicals known to induce DNA damage (e.g. colchicine) were found to have no effect on the life span. The theory was further weakened by the subsequent observations that when certain cells are cultured and grown under laboratory conditions, they show inconsistent responses to radiation exposure.

It is also believed that mutations or alterations in DNA, not exposed to any outside agent like radiation, are too low to account for overall age changes. Further, the primary changes of aging are found to be different from those of radiation treatment. Thus it is concluded by many that this theory cannot explain the basic mechanism of aging.

DNA Damage and Repair Theory : We all use a cycle, or a motorbike or a car to commute from one place to another. Mere usage of the vehicle causes some damage to its parts. The machine could be damaged by outside and unexpected events like accidents. A metal spoke or wire could be broken. If the accident is a major one then severe damage can occur. This kind of wear and tear takes place in cells too. However, there is a difference. Vehicles are inanimate objects. They do not possess an internal mechanism to take care of the damage. We have to take them to a mechanic and get them repaired. However, living cells possess a variety of mechanisms developed over years of evolution to repair the damage that may accrue in their master informational molecule, the DNA. Research has revealed that normally the body DNA-repair mechanisms are quite adequate to take care of any possible damage to the DNA.

In fact the repair mechanisms act with such remarkable accuracy that the DNA molecule is able to, by and

large, maintain its structural and functional integrity, despite an onslaught of outside forces such as radiations or even chemicals produced within the body which can harm the DNA.

The DNA damage and repair theory proposes that the ability to repair the damaged DNA decreases with age in different living systems. As a result, damaged or altered DNA accumulates in cells and all the vital processes like transcription and translation go bizarre with several mistakes and eventually the cell dies. This theory further predicts that the accumulation of DNA damage or decrease in DNA-repair capacity is not a random process but is rather genetically programmed and controlled.

If this theory is to hold true, experimental research must provide evidence for three facts: there should be more and more accumulations of DNA damage in the cells of organisms with chronological age in any case after achieving reproductive maturity; the efficiency of DNA-repair mechanisms must begin to decline with age; longevity of a given species must have a positive correlation with DNA-repair efficiency of their cells.

Indeed extensive research has been carried out to check these important points. In general there is an agreement amongst research workers that more damaged/altered DNA is found in older animals. It is found that cellular DNA from old animals has more breaks in its structure. It is not clear, however, whether this is due to increased incidence of DNA-damaging events in the body or due to a genetically programmed decrease in the DNA-repair capacity or due to both.

Results regarding the age-dependent decline of DNA-repair potential are conflicting. In some experiments it was found to decrease while in some other experiments no effect of age was seen. It appears now that more sophisticated techniques are needed to measure the DNA-repair capacity and scientists are busy at it.

On the other hand, it has been observed by some

researchers that species longevity has a direct relation to their DNA-repair potential. That is, long-lived species, for example humans, elephants, cows have a higher capacity of DNA repair as compared to short-lived animals (rat, mouse, etc.). This is a clear indication that during evolution, some species have acquired a more efficient capacity to keep their genetic apparatus intact and therefore live longer as compared to the rest of the species. This is another aspect to strengthen the view that species longevity is genetically programmed.

Some critics argue that long-living animals (including human beings) may simply have developed an ability to tolerate DNA damage to a higher point than the short-living animals. Also, some higher animals with good

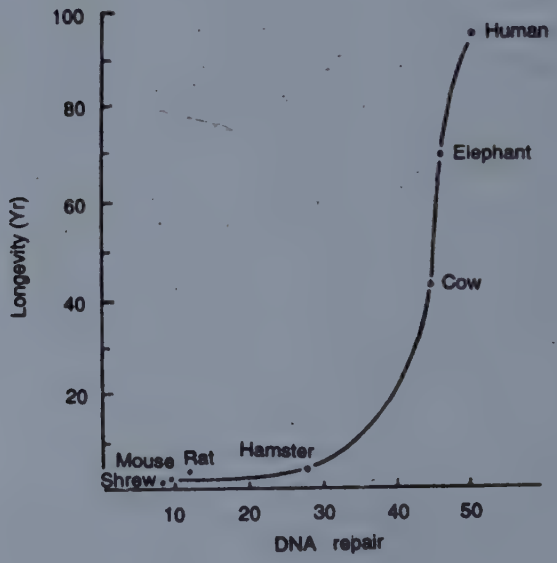

Fig. 13 showing DNA-repair capacity in species with different life spans.

longevity have in their genetic apparatus multiple copies of a given gene. Therefore, even if some genes are affected, some undamaged good genes are available to carry out the prescribed function.

These arguments are answered by supporters of this theory who say that having multiple copies of a gene is genetic, that it has been acquired during evolution, hence they do not take away the basic concept that the integrity of genes (DNA) is of fundamental importance. Organisms which have adapted themselves to maintain this integrity will live longer. DNA damage and repair theory is one of the most accepted ones among the various theories of aging, since the changes found during aging, the variability of life spans in different species, are explainable by this concept at a genetic level. In a way this theory permeates into all other theories of aging.

There are quite a number of other theories to explain why we age. All these are based on the assumptions that certain spontaneous or random events take place in the body which are responsible for either damaging DNA in cells or cause deleterious changes in the vital systems of the body. Since much of the research has already shown that the process of aging has genetic basis, these theories based on spontaneous events do not hold credibility. They attain validity only when such spontaneous events have a genetic control behind them. Some of such theories are the wear-and-tear theory, the error-catastrophe theory, the free-radical theory and the autoimmune theory.

As the names themselves indicate, these theories suppose that general wear and tear, accumulation of errors in vital processes like protein synthesis, damage to cells and DNA by the highly reactive free radical groups and breakdown of immunological systems in the body, are the reasons for aging. As can be seen, all these assumptions may explain some changes taking place in the body with age but cannot explain why the aging process occurs in a programmed and systematic manner

beginning at a discrete point of time during the life span.

However, when these theories are clubbed with DNA damage and repair theory or with the death gene theory, then they seem to explain some of the changes seen in aging. Thus, today, those theories which have a genetic basis—the gene regulation theory, genes responsible for senescence and death and DNA damage and repair—are being studied.

Fig. 14

5

QUEST FOR IMMORTALITY

I never thought that I'd survive
That I'd contrive to stay alive
and whoop it up at ninety-five
But, damn it all, I find that I've
increased the score
to one year more
Wow!
And now you know, it seems to me
That even one full century
need not be necessarily
A real impossibility.

— *Frank Buxton*

In one of the ancient and sacred scriptures of Hindu religion, the *Bhagavad Gita,* Lord Krishna pronounces *"Jatasya hi dhruvo mrityur"* (Death is certain for one who is born)! Every living organism has to die. Except for certain primitive organisms like bacteria which propagate through simple division, all other organisms including us human beings, have to age and subsequently face death.

From birth to death, the events of maturation, reproduction and aging occur in a systematic manner and are genetically controlled. Each individual is born with the instructions embedded deep within the nucleus of each cell. If the whole cycle of events are so inevitable then why study aging at all?

Scientists take up research on aging with three main objectives — to understand the precise mechanisms behind

the changes that occur with age, to know whether these changes can be regulated or controlled by any means so that prolonged longevity can be achieved, and to see if death can be avoided altogether. It is clear that all the outward and cellular changes that occur with age have their root cause at the levels of genes. The genes carry the information about the timing of the age-dependent changes and longevity. In recent years, scientists have provided some direct evidence to prove that aging is indeed a genetically controlled process. Firstly, a gene on the X-chromosome which is otherwise inactive has been found to become 'active' in older individuals. This obviously means that this gene has a role in the onset of senescence. Just three years ago, the gene(s) on chromosome-1 of human beings that is responsible for inducing senescence has been located. When the scientists transferred the chromosome-1 of human cells into a cell line which had been immortalised (these cells keep dividing as long as adequate nutrition is available), the immortalised cells began to show signs of aging. This is a very important discovery which tells us that our chromosome-1 has one or more genes which have the capacity to order the rest of the chromosomes and genes in the cell to stop functioning and start aging.

What is not clear however is how these genes on chromosome-1 and X-chromosome become active. What is the signal that puts them into action? What happens if these genes, through accidents of mutation, become active at a wrong point of the time scale of one's life span?

Indeed, nature itself has provided some answers to these questions. There are atleast four genetic disorders in human beings that are characterised by signs of premature aging. These patients exhibit the features of old age when they are actually 'young' in a chronological sense. These individuals, as can be predicted, die very early. The four genetic syndromes are Down's syndrome, progeria, Werner's syndrome, and Cockayne's syndrome.

The symptoms vary from one syndrome to the other. The common features, however, are premature aging, mental disability and at the cellular level, damaged or altered DNA, probably due to defective DNA-repair capacity.

Down's syndrome, described by a scientist by the name Down, in 1866, is a genetic disorder. One out of every 660 children born is found to inherit this defect. Hence it is one of the best studied and also shows the maximum number of features noticed in normal aging of humans. This defect is due to the presence of chromosome-21 in triplet. Normally we have only one pair of chromosome-21, but in these patients, a third one is also present. This condition is described as trisomy of chromosome-21. The affected person is recognisable very easily because of the 'mongoloid' face.

Progeria, also known as Hutchinson-Gilford syndrome, was first spotted in 1866. It is, however, a very rare disease of early childhood characterised by many of the superficial aspects of aging like baldness, thinning of skin, prominence of blood vessels of the scalp, and vascular disease. These children have the appearance of 'little old men'. They rarely live beyond the age of fifteen to eighteen. Many such cases were found in the following years. The most striking feature in this genetic disorder is severe growth retardation that can be noticed as early as at six to twelve months of age. In these subjects sexual maturation is never reached although in some cases intelligence is found to be normal. Hayflick's limit (the maximum number of doublings that a cell population can undergo under *in vitro* conditions) is only around ten for the cells of these patients as opposed to the normal number of fifty. A progeria patient (Plate V) runs through his entire life cycle at a remarkable pace. Death is usually caused by cardiovascular disease.

Werner's syndrome is similar to progeria in many ways except that the pace at which aging symptoms are developed is much less. Hence these patients usually live

upto their thirties or forties (Plate IV).

The Cockayne's syndrome is one of the recently discovered genetic disorders with signs of accelerated aging. Lack of growth, very little adipose tissue, aged appearance, lack of good intelligence are some of the features (Plate II). The life span is short.

The existence of these genetic syndromes brings forth the fact that aging is a genetic phenomenon. When something goes wrong with one or more of the genes concerned with aging, such syndromes result. Aging is not controlled by just one or two genes but a large number of them. Just as aging itself is characterised by a multitude of symptoms and deficiencies, the number of genes involved with the expression of these features could also be many. Thus, while senescence and aging might lead to death, the varied symptoms of senescence could be brought about by a number of factors.

An interesting question arises from the above discussion. If some mutations could result in disorders that show premature aging, how is it that we do not have any mutations in nature that could lead to no aging at all? A mutation in the positive direction, let us say an alteration in the gene or genes causing senescence, should lead to an immortal person or organism, but that does not happen.

Although there are some reports which claim unusual prolonged longevity in certain regions of the world, these claims are to be taken with some reservation. *Firstly,* their longevities are still within the range of maximum life span of human beings. *Secondly,* it is difficult to imagine how such mutation could take place only in certain regions of the globe and not in other parts.

On the other hand, a more scientific explanation could be given for the absence of immortal human beings. Since the aging process is controlled by many genes, to produce an immortal being, mutations in this direction must occur in all these genes at the same time. This is

a highly unlikely event to occur in evolution because of a sheer probability factor.

However, mutations in the opposite direction could occur in any one of the genes concerned with development or aging and thus accelerate the phenomenon. As a simple example we may consider greying of hair as one of the symptoms of aging. We may also suppose that a particular gene is involved in keeping the hair dark. If an individual inherits this gene in a changed or mutated form, it may lead to greying of hair in that individual very early, even when he is only twenty years old. Thus this could be considered as 'premature aging', in terms of one of the symptoms of aging—in this case the greying of the hair. What happens when a number of genes concerned with the programme of aging are inherited in an altered form? This will be a very rare event but nevertheless possible. It is then that the concerned individual would show many symptoms of aging very early in life and even may face death prematurely. The genetic syndromes mentioned above—Down's syndrome, progeria and Werner's syndrome—fall into this category.

Research on aging is also aimed at examining the possibility of controlling the rate of aging. If the information about how and at what speed one should age resides in genes, should it not be possible to modulate the aging phenomenon through the techniques becoming available today in the field of molecular biology and genetic engineering?

Indeed experiments have already been initiated in this direction. Dr Cleaver's group in San Francisco, USA and Dr Hoeijmaker and his colleagues in the Netherlands have been examining whether the genes concerned with DNA repair can be transferred from DNA-repair proficient cells to DNA-repair deficient cells. The DNA-repair deficient cells are obtained from the skin of patients of a genetic disorder called Xeroderma Pigmentosum (XP). These patients exhibit extreme sensitivity to sunlight.

They harbour a genetic defect concerned with DNA-repair mechanisms and cannot repair sunlight-induced DNA damage in their skin cells. The XP-afflicted subjects also exhibit some signs of premature aging and fall into several categories designated as A, B, C, D, etc. since the defective gene in each group is found to be different—although the ultimate defect is in DNA repair.

The scientists have achieved what is described as fusion of cells, obtained from one XP-group of patients with those obtained from a different XP-group. Some of the resulting hybrid cells have gained the DNA-repair proficient character and behave like normal cells. This means that the XP-cells from two different groups, deficient in DNA repair by themselves because of the defect in two different genes, have complemented each other so that the progeny cell has become normal.

This is like two persons having plates of meals before them. One of them has all the items except rice, the other has all the items except curds. The first one donates some curds to the second while the second donates some rice to the first. Both, now, have a complete meal!

Some human DNA-repair genes have been identified and found to be quite similar to those already characterised in lower organisms like bacteria. Attempts are on, with already some success, to transfer lower organism genes into DNA-repair deficient human cells. Scientists in the Netherlands have used the technique of micro-injection for this purpose. The technique involves injection of the genes into a single cell using a very fine micro-needle. Research is progressing very rapidly in this direction. In all these experiments it is assumed that DNA-repair capacity is at least one of the factors contributing towards longevity.

One question that entertains the minds of scientists, is whether we can achieve immortality like the *devatas* in the Hindu epics! In principle, we have already seen that aging may not be an inevitable property of all biological

systems. For example, a germ cell (sperm or ovum) can be considered as a potentially immortal cell. When these two fuse to form a zygote, the zygote can develop into a full organism again capable of reproducing through the germ cells. Similarly, many micro-organisms like bacteria and protozoa can endlessly keep dividing as long as the nutrients are available. Also, a cancerous cell is essentially immortal; it keeps dividing while taking away the nutrients from the neighbouring cells. In fact, several cell lines cultured in laboratories and converted into immortal ones by treatment with some chemicals are available today.

All this means that immortality, whether desirable or not, is not an impossibility. What is important is that immortality is to be obtained not in the form of a disease, like cancer, but as a natural and normal phenomenon. The cells should remain live and normal but not as cancerous cells. Somewhere there is a subtle directional change between immortality, aging and cancer.

However, the aim of the aging research is not to achieve immortality—at least it is not one of the immediate primary concerns. What is important to be achieved, according to many gerontologists, is a 'healthy aging'. Customarily old age is viewed as an unwanted part of the life span characterised by dejection, frustration, lack of companionship, failing health and unwantedness. If the understanding of the aging process can lead to elimination of the diseases and ill-health associated with old age, it would serve a most humane purpose. Then people can 'age' in a healthy and happy manner. Of course, death will finally take over, but it need not necessarily be preceded by a prolonged illness and debilitative life. Life has a beginning, middle and an end. Why should the end be a miserable and dreaded one always?

Some people have not given up the immortality bid altogether either. The lure of immortality is very powerful. Many people in countries like America have paid large sums of money to deep-freeze their bodies after death,

with the hope that there will one day be a biotechnological miracle capable of bringing them back to life. Some are, according to one report, seriously considering the possibility of having themselves frozen before death with the hope that they can be revived at some future date when their bodies could be rejuvenated.

In fact the idea of freezing human bodies was popularised by one R.C.W. Ettinger in his book, *The Prospect of Immortality,* published almost thirty years ago. Cryonics Society of California, USA, has taken up the task of freezing dead bodies.

Fig. 15.

6

THE AUTUMN OF LIFE

Grow old along with me
The best is yet to be
The last of life,
for which the first was made.

— Robert Browning

It is seen that the aging process is multi-disciplinary in nature. It results from a complex interplay of physiological, psychological and social factors. It is, however, essential for us to realise that inheritance of longevity in humans is more difficult to ascertain as the life span is influenced by socio-economic and other environmental factors too. Limitations of the elderly can be remedied by changes in social customs, so that much can be done to improve the status of the aged. The adaptability of the human organs makes it possible to compensate for many of the physiological impairments of aging. A number of studies reveal that the life span is influenced to a considerable degree by heredity or susceptibility to major diseases like cancer and heart disease running in the family. Similarly there is strong evidence to suggest that monozygotic (genetically identical) twins tend to have similar life spans than do like-sex dizygotic (fraternal) twins.

Because of the improvement in general medical care and reduction in infant mortality, there is notable increase in the longevity of populations all over the world. The improvements in the developed world such as the USA

and the countries of Europe are more spectacular than in a developing country like India.

Still, the average life span of an Indian has gone upto fifty-nine years from around thirty-five years as evident forty years ago. Indications are that this trend will continue because of the medical advances and adoption of more hygienic practices coupled with family planning. This means that there are more and more older people in the population. In 1980 about 11.2 per cent of the total population of United States was over sixty-five years old. This, in absolute figures amounts to twenty-five million persons. It is projected that by the year 2000 this figure will rise to thirty-five million and by the year 2030 to sixty-five million.

In a country like India where the total population is almost five times that of United States, even a small percentage of people over sixty or sixty-five years would constitute a big number. Today about fifty million people are above sixty years of age in India and this makes about 6 per cent of the population. According to one comparison, the number of elderly people (more than sixty years in age) in developing countries alone would soon be equal to all the population in the developed world!

What would be the consequences of such changing compositions of the world populations? The consequences could be socio-psychological, economical and even political. In the olden days, when older persons in a given family or society were few, they commanded respect and the decision-making powers was in their hands. Wisdom was always associated with the old—therefore, their judgments were accepted without questioning. A famous quotation says that *'no wise man ever wished to be younger'*. Youth has always been associated with vigour, vitality, haste and an attitude of 'now or never'. On the other hand, older people, with their vast past experience, may tend to weigh things in a proper perspective and come to more realistic and long-lasting conclusions.

What happens when such 'wise' population increase in proportion in a given society? It is possible that such a nation or society would be greatly benefitted by such competent and wise population—provided they are made use of by the nation. It is also possible that with limited opportunities, there may be a competition amongst the 'old' themselves not to talk of their conflicts with younger generations. The 'youth' and the aged may look at each other as competitors rather than complementing factors.

Age itself is no bar to creativity, and many major achievements in the arts and sciences have been reported for persons with advanced age; but surveys abroad reveal outstanding achievements in mathematics, physics and biology are primarily made by individuals in their thirties than in their sixties. On the other hand, achievements in politics, administration and religion—areas in which experience is a dominant factor—are most likely to occur

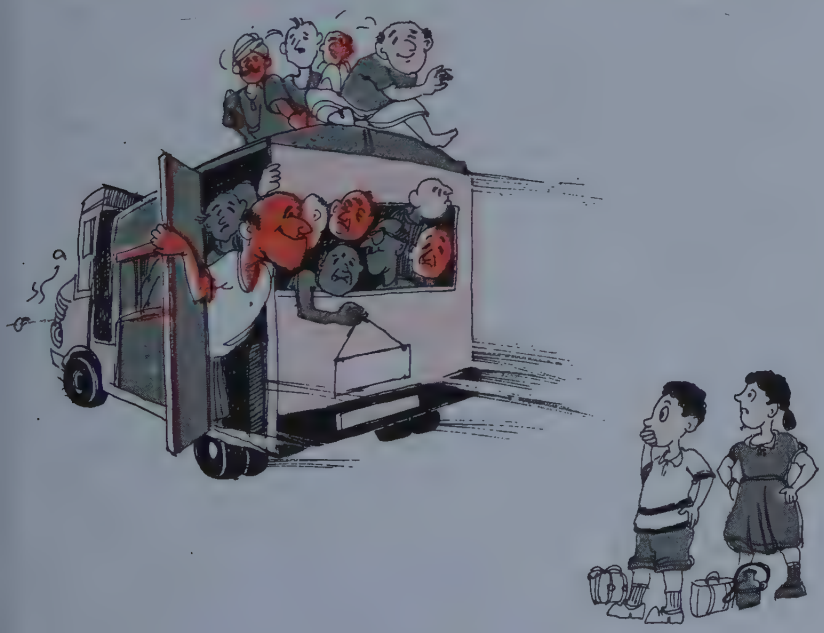

Fig. 16.

later in life as is evident in our country.

Aged people tend to become more cautious and rigid in their behaviour and to withdraw from social contacts. These behaviour patterns may be the result of social institutions and experiences rather than an intrinsic phenomenon of aging. Many persons who 'age successfully and gracefully' make conscious efforts to maintain mental alertness by continued learning and by expansion of social contacts with individuals of a younger age group. Maintenance of a broad spectrum of activities and interests is essential for proper adjustment in old age. Two other factors that are helpful in this respect are good health and an adequate income.

With advances in longevity and medicare to assure a healthy old age (with the pre-death suffering period reduced to a minimum), the above possibilities may become a reality in future in many countries. Therefore the State has to plan carefully in order to use the 'youth' and 'old' as synergistic forces.

It is also essential that a new social and cultural fabric be inducted into the societies. Luckily in India this would be an easy task because of its cultural heritage. The old must know that youth was their past. The youth must know that their future is old age. The past must be revered and the future looked forward to. In the words of Sarvepalli Radhakrishnan: *"The blossom cannot deny the leaf, the leaf cannot deny the stalk nor the stalk, the root."*

7

CONCLUSION

The process of aging is genetically programmed. Every organism which has opted for sexual reproduction to provide hybrid vigour and vitality to the offspring, has also to die after performing the reproductive function. This information is written down in the fertilised egg itself in the language of DNA, RNA and protein. However, during the course of evolution different species acquired different life spans and these differences are largely due to the different lengths of time taken to reach reproductive maturity and the length of reproductive span itself. Thus long-living species like human beings take considerable time to attain maturity. Similarly the period of their reproductive capacity is also significantly long.

There is mounting experimental evidence to show that the process of aging sets in at some point of the reproductive phase. The biological clock rings and unwinding of the spring starts—resulting in a progressive deterioration of all physiological activities with time. These deteriorative changes are seen at all levels including the visible. At a critical point of this overall decline, death ensues. Since the basic command affecting these changes lies at the level of genes, it is important how well the integrity of genetic apparatus is maintained.

There are individual differences in this capacity—a trait which is also inherited. It is this factor as well as outside factors like diet and radiation that tend to contribute towards differences in the life spans of individuals. Nevertheless, the maximum life span of a given

species is fixed at least at this point of evolution.

Rapid strides in biological research promise that genetic intervention of the aging process is a possibility. What could perhaps be achieved in the years to come is to improve the longevity to the point of a maximum life span. Further and more importantly, to reduce the suffering before the inevitable death, so that people can age happily.

Glossary

absorption : the act of imbibing; taking in; incorporating.

adaptation : the act, process or results of anything which are adjusted to conditions.

adipose tissue : the vesicular or sac-like structure in the animal body which contains fat.

ailment : pain; indisposition; disease, especially if not serious.

Alzheimer's desease : a form of age-associated disease characterised by senile decay.

amino acids : basic unit of proteins.

anabolic : synthesis of complex substances in living organisms.

androgens : male sex hormones.

anaemia : bloodlessness; lack of red blood corpuscles or of haemoglobin—a condition marked by paleness and languor.

animate : living.

artery : tube or vessel that conveys blood from the heart.

arteriosclerosis : hardening of the arteries.

arthritis : inflammation of a joint; gout.

asexual : without sex; not involving sexual activity; vegetative.

atrophy : wasting away; degeneration; diminution of size and functional activity by disuse; emaciation.

bacterium : a class of unicellular organisms, cause of many diseases; *pl.* bacteria.

basal ganglia : a nerve centre of brain situated at the lowest level or base of the skull.

beget : to produce or cause; to generate.

bronchi : *sing.* bronchus; the main fork of the windpipe.

bronchitis : inflammation of the lining of the bronchial, or airway tubes.

cardiac : relating to heart.

cartilage : firm, elastic substance covering the joint in animal bodies.

catalyst : substance that aids or speeds up a chemical process but does not itself undergo any change.

cataract : an opaque condition of the lens of the eye, painless, unaccompanied by inflammation.

chromosome : rod-like portion of the chromatin of the cell nucleus.

chronic : lasting a long time; deep seated or long continued.

chronological : in order of time.

ciliary muscles : contraction of which alters the curvature of the lens and helps in accommodation to light.

Cockayne's syndrome : a genetic disease involving sensitivity to ultraviolet light, mental retardation, premature aging, and dwarfism.

codon : a set of three bases in the messenger

RNA which determines a particular amino acid in protein synthesis.

collagen : a protein in fibrous connective tissue.

complementary : completing, together making a whole.

composition : the nature or proportion of the ingredients of anything.

conduction : act of carrying or transmitting.

confluence : flowing together; the act of meeting together.

conjugation : temporary or permanent union of two cells or individuals.

connective tissue : tissue binding together; to associate or establish a relation between various other parts.

contraction : a tightening of the muscles or muscle fibres.

crossing over : interchange of parts of two chromosomes when they separate.

debility : weakness.

degenerate : to be or to grow worse.

dementia : a form of insanity characterised by the failure or loss of mental powers; organic deterioration of intelligence, memory, and orientation.

deoxyribonucleic acid : nucleic acid containing deoxyribose (sugar), present in chromosomes of all plant and animal cells, and carrying in coded form instructions for passing on the hereditary characteristics; *abbrev.* DNA.

diabetes : disease in which sugar cannot be properly utilised.

diploid : cell having the normal double

complement of genetic material.

dizygotic : developed from two zygotes or two fertilised eggs.

dormant : in a state of inactivity but awaiting development or activity.

Down's syndrome : mongolism; characteristic facial appearance with mental retardation.

dysfunction : impairment or abnormality of the functioning of an organ.

elastin : a protein, chief constituent of elastic tissue.

eliminator : one who or that which eliminates.

embryonic : offspring of an animal in the early stage of development before birth.

emphysema : an unnatural distension of a part of the body with air; distension of the lung, with breathing difficulties.

endocrine : secreting internally; applied especially to certain glands that pour secretions into the blood; ductless glands.

environment : surroundings; circumstances; influences.

enzyme : any one of a large class of protein substances produced by living cells which acts as a catalyst.

estrogens : female sex hormones.

fertility : fruitfulness; capable of breeding, hatching or germinating.

fibroblasts : a cell in connective tissue from which fibrous tissue is formed.

fission : a cleaving; reproduction by dividing; splitting up of the nucleus into roughly two equal parts.

fluidity : unsolidified state; likely to, tending to change; easily changed.

foetal : relating to the usual but entomologically unsatisfactory form of the young animal in the egg or in the womb, after its parts are distinctly formed.

fraternal : dizygotic; arisen from two independently fertilised cells.

gamete : a sexual reproductive cell; an ovum or sperm.

gamma-rays : a penetrating radiation given off by radium and other radioactive substances; *abbrev.* γ-rays.

generation : a single stage in natural descent; the people of the same age or period; descendants removed by the same number of steps from a common ancestor; offspring; progeny; race.

genes : one of the units of DNA, arranged in linear fashion on the chromosomes, responsible for passing on specific characteristics from parents to offspring.

genetic engineering : a biological science whose aims include the control of hereditary defects by modification or elimination of certain genes, and the mass production of useful biological substances by the transplanting genes.

genetics : science dealing with heredity; the ways in which characteristics are passed on from parents to offspring.

genome : the full set of chromosomes of an individual; the total number of genes in such a set.

gerontology : the scientific study of the processes of growing old.

gravity : weightiness; gravitational attraction or acceleration.

haploid : set of chromosomes containing one copy each of all chromosomes characteristic of the species, as in germ cells.

Hayflick's limit : maximum number of doublings that a population of cells can undergo under laboratory conditions.

helical : a screw-shaped coil.

homologous : of the same essential nature; corresponding in relative position; general structure and descent.

hormones : an internal secretion which on reaching some part of a plant or animal body exercises a specific physiological action.

hybrid : inter breed, or from parents of different species or varieties.

hygiene : the science or art of preserving health; sanitary principles.

immortal : exempt from death; imperishable; one who will never cease to exist.

immunological : which helps in defence mechanism; rendering a person not liable to danger, especially infection or disease causing germs.

impairment : to injure or weaken; unsuitable; unfit or inferior.

impermeable : not permitting passage, especially of fluids; impervious.

impulse : a beat or wave travelling along a nerve or muscle.

inanimate : lifeless.

incidence : the frequency or range of occurrence.

infant : a child during the first few years of its life.

inhalation : the act of drawing into the lungs.

inherit : derive from ancestors.

initiate : to begin; start; to perform the first act.

insoluble : not capable of being dissolved.

insomnia : sleeplessness; prolonged inability to sleep.

intercellular : place among or in between cells.

in vitro : in glass; in the test-tube; under laboratory conditions.

irradiation : treating by exposure to rays.

juvenile : characteristic of a young person; in early life.

lean body mass : flesh without fat.

longevity : long life.

malfunction : the act of working or functioning imperfectly.

malignant : tending to cause death, or go from bad to worse, especially cancerous.

maturation : a bringing or a coming to maturity; the process of suppurating fully.

meiosis : cell division with reduction in the number of chromosomes towards the development of a reproductive cell.

menopause : the ending of menstruation; change of life.

messenger RNA : a type of RNA that carries information of the genetic blueprint [DNA] from

the cell nucleus to the ribosomes [protein synthesising bodies], where the code is translated to protein.

metabolism : the sum total of chemical changes of living matter.

milestone : stage or event in a human life.

mitotic division : an elaborate process of cell division involving the arrangement of protoplasmic fibres in definite figures.

mongoloid : showing characteristic features of mongolism: a congenital disease caused by chromosomal abnormality, in which there is mental deficiency and a broadening and flattening of the features; now more usually called *Down's syndrome.*

monolayer : is composed of a continuous single layer.

monozygotic : developed from one zygote.

morphology : external description of animals and plants.

mortality : number of deaths or death rate.

multicellular : having or made up of many cells.

mutation : changes or alterations in characteristics or functions.

myopia : shortness of sight.

neurons : nerve cells.

nucleic acids : complex acid components of nucleus.

nucleotide : a nitrogenous base with sugar linked by phosphate; forms the basic unit of nucleic acids.

nutrition : the act or process of nourishing; food.

obesity : abnormal fat.

offspring : a child; progeny.

olfactory : pertaining to, or used in smelling.

onset : visible start.

optic : relating to sight or to the eye.

osteoporosis : loss of bony tissue; resulting in bones that are brittle and liable to fracture.

ovum : female germ or sex cell in animal capable of developing into a new individual when fertilised by a male sperm.

paralysis : loss of feeling or power to move in any or every part of the body.

Parkinson's disease : a disorder of middle age and elderly people characterised by tremor, rigidity and a poverty of spontaneous movements.

passage : the state of repeated culturing of cultured organ cells in the laboratory.

peptides : a molecule consisting of two or more amino acids linked by bonds between the amino ($-NH_2$) group and the carboxyl group (-COOH). This bond is known as *peptide bond.*

physiological : relating to the science of the processes of life in animals and plants.

physiology : science of the normal functions of living things.

plasmid : it is an autonomous self-replicating extra chromosomal circular DNA.

plateau : a flat region.

polymerisation : process of combining to form a more complex molecule.

polynucleotides : many nucleotides joined together.

post-natal : after birth.

prebiotic : period before life began.

predators : living by prey.

premature : unduly early.

progeny : descendants; offsprings.

progeria : a very rare condition in which all the signs of old age appear and progress in a child, so that senility is reached before puberty.

propagation : increase in the number by natural processes from the parent stock; or reproduce.

proteins : any member of a group of complex nitrogenous substances that play an important part in the bodies of plants and animals.

protoplasm : colourless, jelly-like substance which is the material basis of life in animals and plants.

protozoa : the lowest and the simplest of animals; unicellular forms or colonies multiplying by fission; *sing.* protozoan.

purines : a nitrogen containing compound with a two-ring molecular structure, which forms the nucleotides of nucleic acids.

pyrimidines : a nitrogen-containing ring molecular structure which forms the nucleotides of nucleic acids.

radiation : the emission and diffusion of rays; energy transmitted in electromagnetic waves.

recombination : to join together again; recombinant genetic material produced by the combining of the different DNA molecules.

rejuvenate : make or become young or vigorous again in nature or appearance.

replication : doubling or copying itself for increase in number.

repression : being kept; or put down; or under.

reproduce : bring forth as offspring; bring about a natural increase.

respiration : breathing; the taking in of oxygen and giving out of carbon dioxide, with associated physiological processes.

ribonucleic acid : nucleic acid containing ribose sugar occurring in the nucleus and cytoplasm of the cells; *abbrev.* RNA.

ribose : it is pentose [5 carbon] sugar found in RNA and DNA.

secretion : a mass of mineral matter formed by inward growth in a cavity; that which is secreted.

seizures : sudden attack of apoplexy or stroke; convulsions.

senescence : signs of old age.

senile dementia : loss of intellectual faculties, beginning for the first time in old age.

senility : suffering from bodily or mental weakness because of old age.

sensitivity : more than usual irritability.

somatic : relating to non-reproductive parts of the body; relating to body wall.

species : group having some common characteristics.

sperm : male germ or sex cell in animals that fuses with female sex cell during fertilisation.

spore : a small reproductive body produced by plants and micro-organisms.

stem cells : the main or origin cells which give rise to many cells of a certain line or family.

stimulus : an action, influence or agency that produces a response in a living organism.

stochastic : random.

stroke : an attack of apoplexy or of paralysis.

susceptibility : easily affected; capable of being attacked by infection or disease causing germs.

symptoms : indication of change in the body's condition.

syndrome : a characteristic pattern or group of symptoms indicative of a problem or condition; disease.

synergistic : combined or coordinated action; working together; a substance which increases the effect of another.

synthesis : building up; putting together; making a whole out of parts; the combination of separate elements.

template : pattern or gauge used as a guide.

tendon : tough, thick cord that joins muscles to bones.

thymus gland : bilobed ductless gland in the root of the neck, above and in front of heart. In infancy the thymus controls the development of immune response to microbes and foreign proteins.

trait : distinguishing quality or characteristic.

transcription : synthesis of RNA using DNA template.

transform : change the shape, appearance, quality or nature.

translation : the protein of protein synthesis in the cells with the help of message coded in the mRNA.

tremor : a quiver; an involuntary agitation; a vibration.

ultraviolet light : *abbrev.* UV : invisible short-wave length radiation beyond violet end of the visible spectrum. Sunlight contains UV-rays.

unicellular : describing organism or tissues that consist of a single cell, e.g. most bacteria and some fungi.

vascular : vessels or ducts through which blood or sap flows.

Werner's syndrome : a genetic disease with clinical features that resembles premature or accelerated aging including marked lymphoid depletion, glucose intolerance, cataract, greying of the hair and increased incidence of arteriosclerosis and cancer.

Xeroderma Pigmentosum : a genetic disease which impairs DNA-repair mechanism resulting in sensitive skin to UV irradiation and prone to skin cancer resulting from exposure to sunlight; *abbrev.* XP.

X-rays : electromagnetic radiation of extreme short-wave length (beyond UV) with great penetrating powers in the matter opaque to light.

zygote : the fusion product during sexual reproduction.

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The human body does not remain at the peak of its powers endlessly. A gradual decline sets in after maximum efficiency has been achieved. This normal process of aging occurs due to the complex interplay of physiological, psychological and social factors. Written in simple and lucid language, this book explains why and how every organism which has opted for sexual reproduction must die after performing the reproductive function.

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